REMARKS

Upon entry of the present amendment, claims 6, 13-17, and 19-25 are pending in this application. Claims 1-5, 7-12, 18 and 26-34 are cancelled. Claims 6, 19 and 20 are amended herein. Claim 6 is amended to correct the antecedent of "target gene" as requested by the Examiner. Claims 19 and 20 are amended to recite the phrase "an inverted" positive or negative regulatory element that, upon inversion by the recombinase, results in either activation or inactivation, respectively, of the target gene. Support for the amendments made herein can be found at least at page 7, lines 9-17. As such, no new matter is added.

Claim Rejections under 35 USC §112

Claims 19 and 20 are rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement.

Claims 19 and 20 are amended herein. As such, Applicants submit that the rejection has been overcome. Reconsideration and withdrawal are requested.

Claims 6, 13-17, and 19-25 are rejected under 35 USC §112, second paragraph, as being indefinite.

Claim 6 is amended herein. All remaining claims subject to the rejection properly depend from amended claim 6. As such, Applicants submit that the rejection has been overcome. Reconsideration and withdrawal are requested.

Claim Rejections under 35 USC §103

Claims 6, 15-17, and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moller et al. US Patent No. 6,723,893 B1, herein referred to as "Moller," in view of Odell et al. US Patent No. 5,658,772, referred to as "Odell." Applicants traverse the rejection with respect to the pending claims as amended herein.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim

limitations. Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Moreover, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one ordinary skill in the art. *See* MPEP §2143.01, citing *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385, 1396 (2007).

For clarity purposes, Applicants are describing the teachings of the cited references individually but are traversing the rejection with respect to the combination of these references as described in further detail below.

Applicants submit that Moller fails to teach all the essential elements of pending independent claim 6 (and therefore, all essential elements of those claims which properly depend therefrom and necessarily include the limitations of independent claim 6). As stated by the Examiner at page 10 of the Office Action, Moller fails to teach the inclusion of signal sequences recognized by the recombinase in the first nucleic acid molecule such that the expression of the recombinase excises a sequence from the first nucleic acid molecule resulting in modulation of the recombination gene. The Examiner states, however, that it would have been obvious to combine the construct described in either Figure 1 of Moller with the suicide constructs, depicted in Figures 4 and 5 of Moller, in order to create a self-excising recombinase (see Office action at page 11). Furthermore, the Examiner states that the explicit motivation to combine the Moller constructs to create a self-excising recombinase, is the ability to specifically remove transgenes from transgenic plants as a way of introducing desired traits without the presence of potentially environmentally unfriendly transgenes such as antibiotic resistance markers (see office action at page 11). Applicants contend that the desire to introduce genetic traits into crop species without the presence of environmentally unfriendly transgenes, as taught by Moller and cited by the Examiner, does not provide explicit or implicit motivation to combine the constructs of Moller in order to create a self-excising recombinase. Moller does not teach or suggest that the presence of the recombinase within a transgene is environmentally unfriendly. As such, Applicants submit that this statement cannot provide motivation to combine the constructs of Moller in order to create a self-excising recombinase, because the result would predictably not satisfy the intended outcome.

Applicants further contend that the combination of constructs taught by Moller, can not be obvious to one of ordinary skill in the art because Moller did not combine these structures. Applicants submit that the authors of Moller represent highly skilled persons in the art having all of the required elements and knowledge readily available to combine the constructs that they generated. However, even the authors of Moller, as highly skilled artisans, failed to recognize that the combination was desirable or possible. Applicants further submit that if a highly skilled artisan fails to combine these elements, provided the same theoretical motivation as the ordinarily skilled artisan and greater access to the required reagents, then the combination must not be obvious to one of merely ordinary skill in the art.

Moller also fails to teach or suggest the incorporation of regulatory elements, either positive or negative, into one or more nucleic acid sequences of the invention. Moller fails to teach or suggest placing regulatory elements in an inverted orientation with respect to a promoter element or a target gene. Moller does not teach or suggest modification of target genes expression by inverting either a positive or negative regulatory element of a target gene. As such, Moller necessarily fails to teach or suggest activation or inactivation of a target gene by inversion of an inverted positive or negative regulatory element in the second nucleic acid molecule. Odell fails to correct the deficiencies of Moller.

Applicants submit that Odell fails to teach all essential elements of the invention. Specifically, Odell fails to teach or suggest the introduction of a recombinase gene that is flanked by signal sequences recognized by the recombinase. Odell also fails to teach or suggest that the expression of the recombinase gene results in excision of the recombinase. Odell merely teaches that site-specific recombination of DNA at the points of introduced lox P sites can occur in a variety of ways, including "inversion of the nucleotide sequence of the DNA segment flanked by lox sites (flipping)" (column 9, lines 59-65). Odell further states at column 10, lines 17-20, "Gene expression can be turned on by changing the direction of a promoter or regulatory nucleotide sequence from an inactive to an active orientation with respect to a coding region."

However, Applicants further submit that Odell provides evidence that activation of the target gene by the above-described flipping mechanism does not yield predictable results. Odell describes a failed attempt to invert a construction, in which coding and polyadenylation regions from a sulfonylurea-resistant ALS gene were placed between two synthetic loxP sites that were in inverted orientation relative to each other (see, column 9, lines 26-56). In this construction, the lox-P bounded fragment was placed in inverted orientation to the 25S promoter such that it

would not be expressed. Odell states that this construction was "defective in some as yet undetermined aspect." Applicants submit that if the working examples relied upon to provide guidance to one of ordinary skill in the art ultimately demonstrate that the elements or methods to be substituted are unpredictable, then the skilled artisan has no reasonable expectation of predictable results when substituting the elements and methods of Odell for the method of Moller in order to reach the present invention. Moreover, Odell provides no explanation for the failure of this construction, and thus, no guidance that would enable the ordinarily skilled artisan to confirm or ensure predictability of the method to be substituted.

The Examiner states at page 9 of the Office action that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute activation of the target gene by inversion of a regulatory nucleotide sequence for activation by inversion of the target gene in the second nucleotide sequence as taught in the method of Moller. The Examiner further states that the substitution would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention. Applicants disagree and contend that Odell introduces unpredictability into the combination or modification of the teachings of Moller and Odell. As such, Applicants submit that one of ordinary skill in the art, provided the disclosure of Odell, would not be motivated to substitute the failed and unpredictable method of inverting regulatory elements and/or target genes for the method of Moller in order to reach the present invention with any expectation of predictable results or success.

For all of the foregoing reasons, Applicant submit that the present invention is nonobvious over the teachings of Moller in view of Odell, when considered either alone or together. As such, Applicants request reconsideration and withdrawal of the rejection.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moller in view of Odell, and further in view of Baszczynski et al. US Patent No. 6,187,994, herein referred to as "Baszczynski." Applicants traverse the rejection with respect to the pending claims as amended herein.

Claim 13 properly depends from independent claim 6, and as such, contains all of the limitations of claim 6.

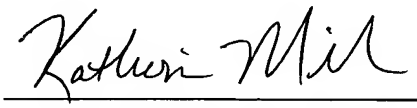
Applicants submit that the invention as described by claim 13 is nonobvious over Moller in view of Odell for the reasons stated above. Baszczynski fails to correct the deficiencies of Moller and Odell. Baszczynski merely teaches that cre/lox systems can be used to express

disease resistance genes. Baszczynski fails to teach or suggest essential elements of independent claim 6, and thus, essential elements of the invention as described by claim 13. Specifically, Baszczynski fails to teach or suggest excision of the recombinase or inversion of a target gene or regulatory element. Applicants submit that for all of the foregoing reasons, the teachings of Moller, Odell, and Baszczynski, either taken alone or together, cannot be combined or modified to reach the invention described by claim 13. Applicants request reconsideration and withdrawal of the rejection.

CONCLUSION

On the basis of the foregoing amendment and remarks, Applicants respectfully submit that the pending claims are in condition for allowance and a Notice of Allowance for the pending claims is respectfully requested. If there are any questions regarding this application that can be handled in a phone conference with Applicants' Attorneys, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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